
بسم الله الرحمن الرحيم

7th Lecture

Kidney Function Tests

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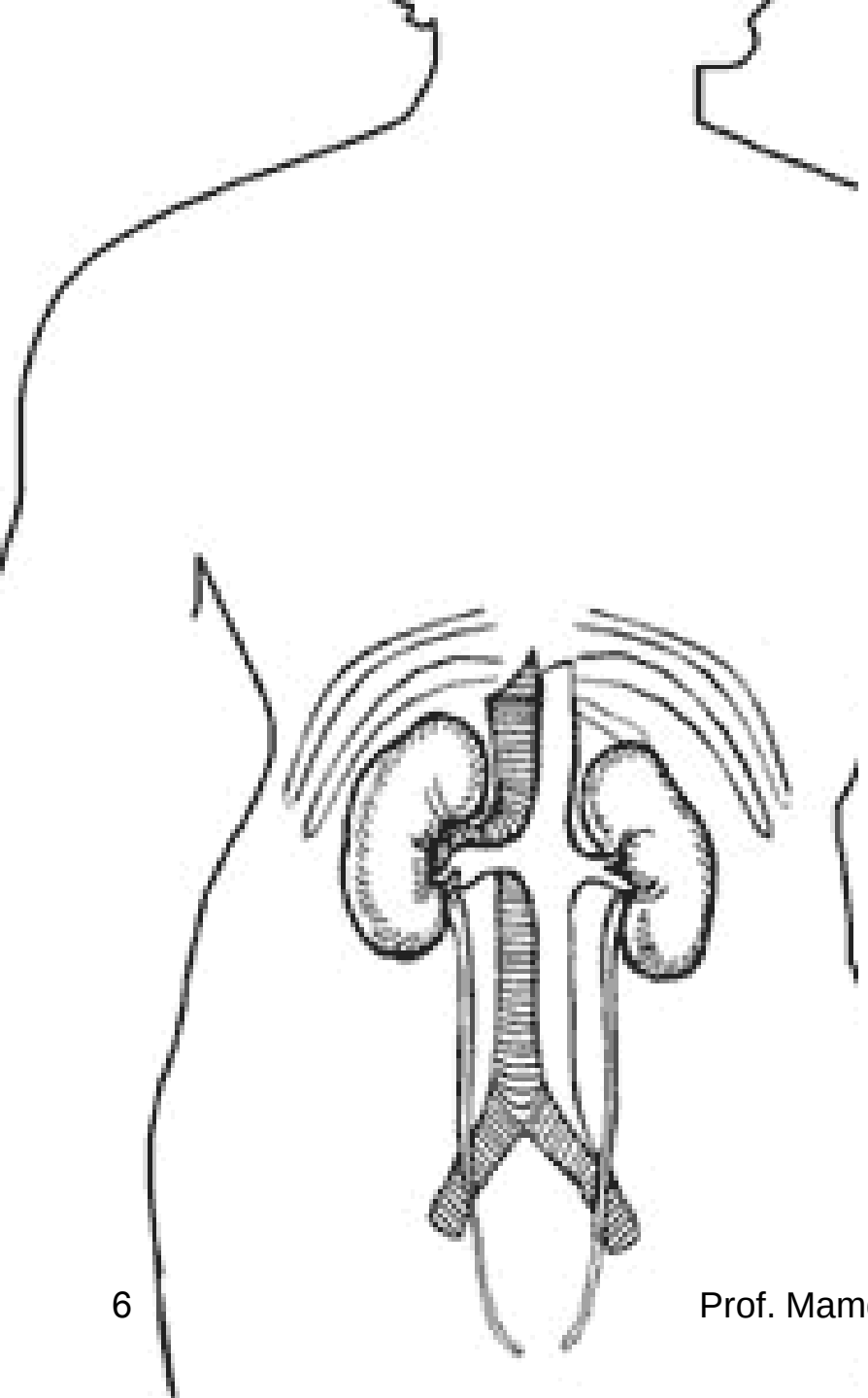
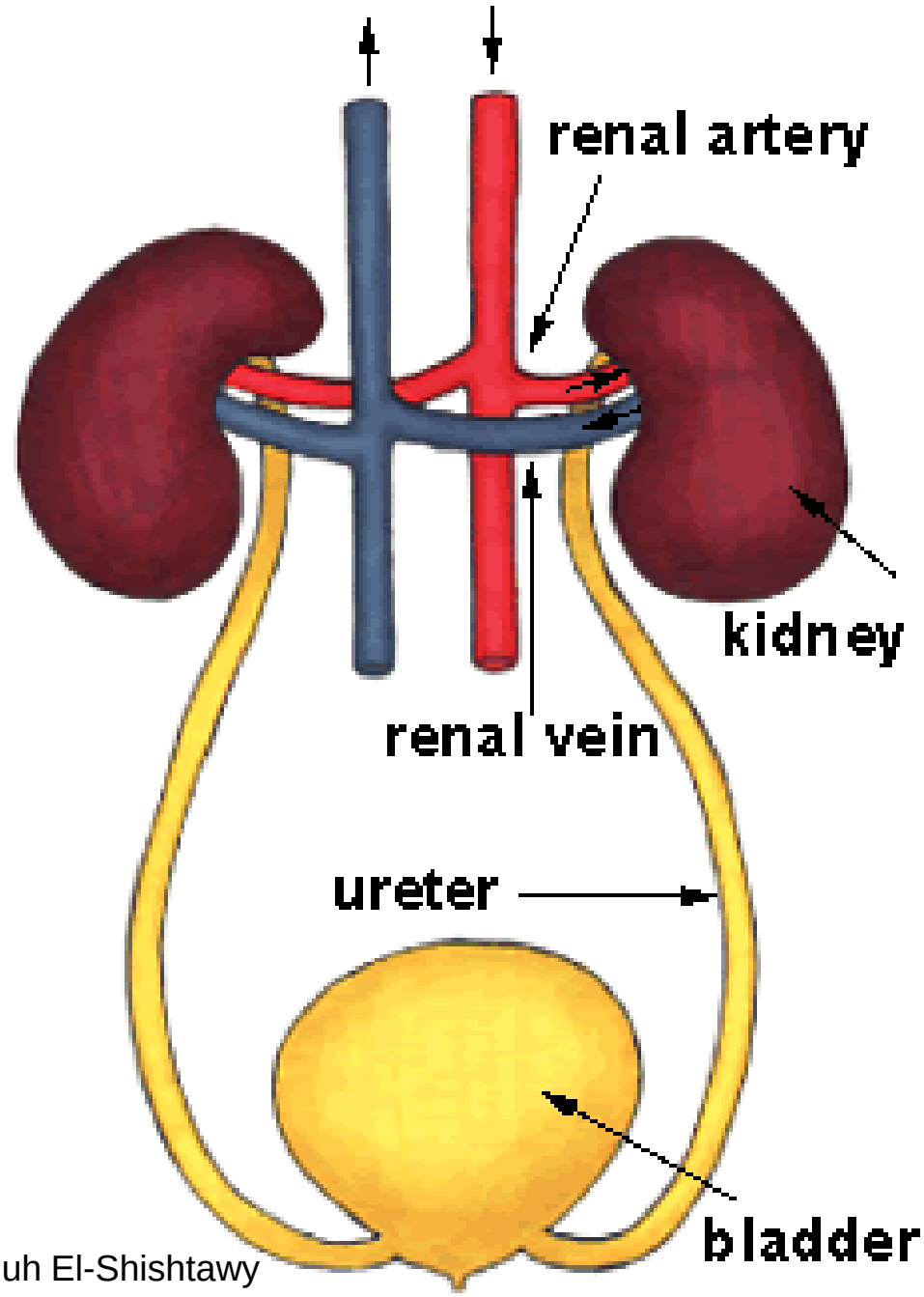
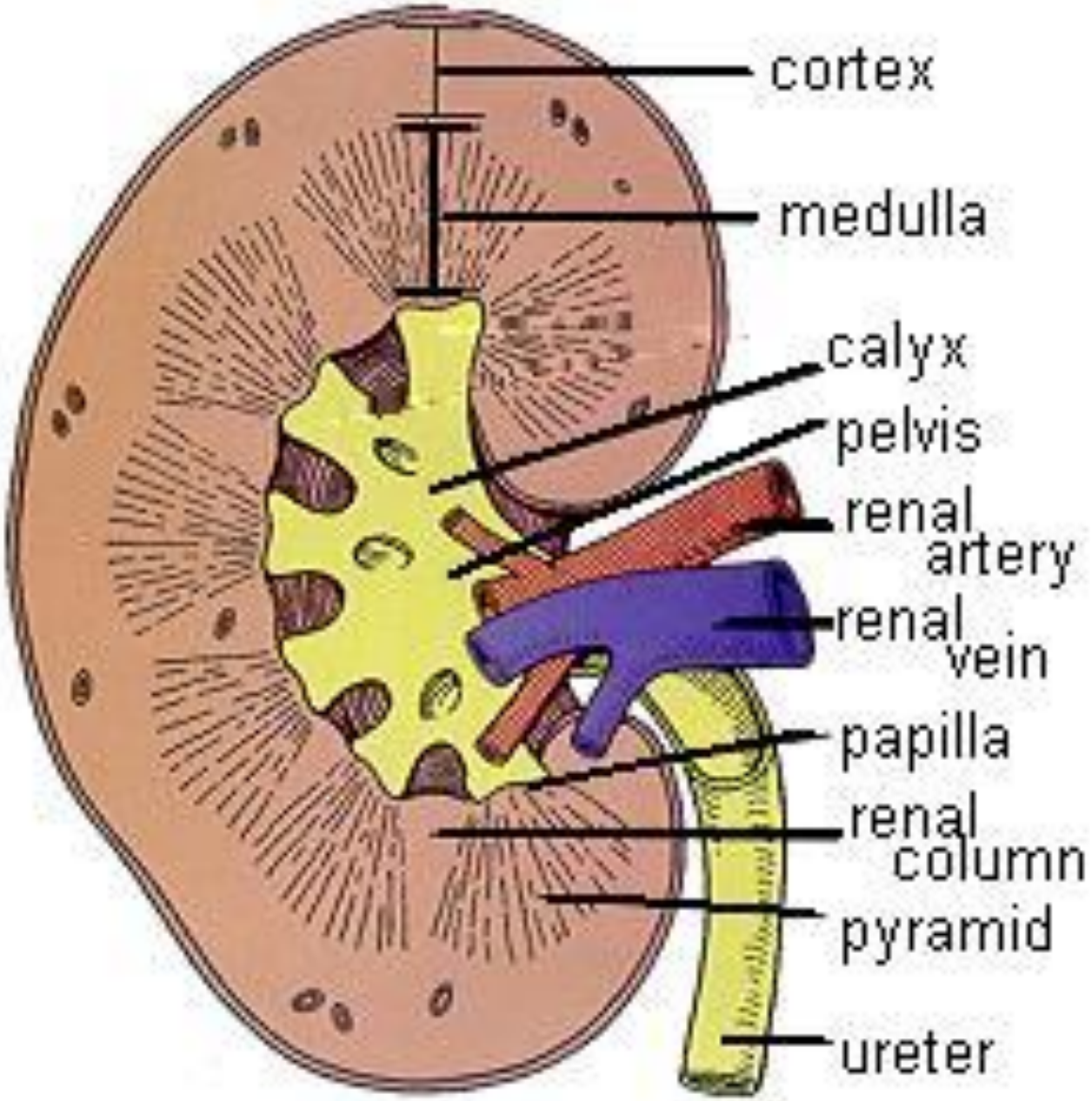
The Urinary System




renal artery
kidney
renal vein
ureter
bladder

Review of Kidney

- Kidneys are a pair of fist-sized (بحجم قبضة) organs located outside the peritoneal cavity on each side of the spine.
- Together with the skin and the respiratory system, kidneys are the body's primary excretory organs.
- Kidney is a highly specialized organ that maintains the internal environment of the body by selectively excreting or retaining various substances according to specific body needs.

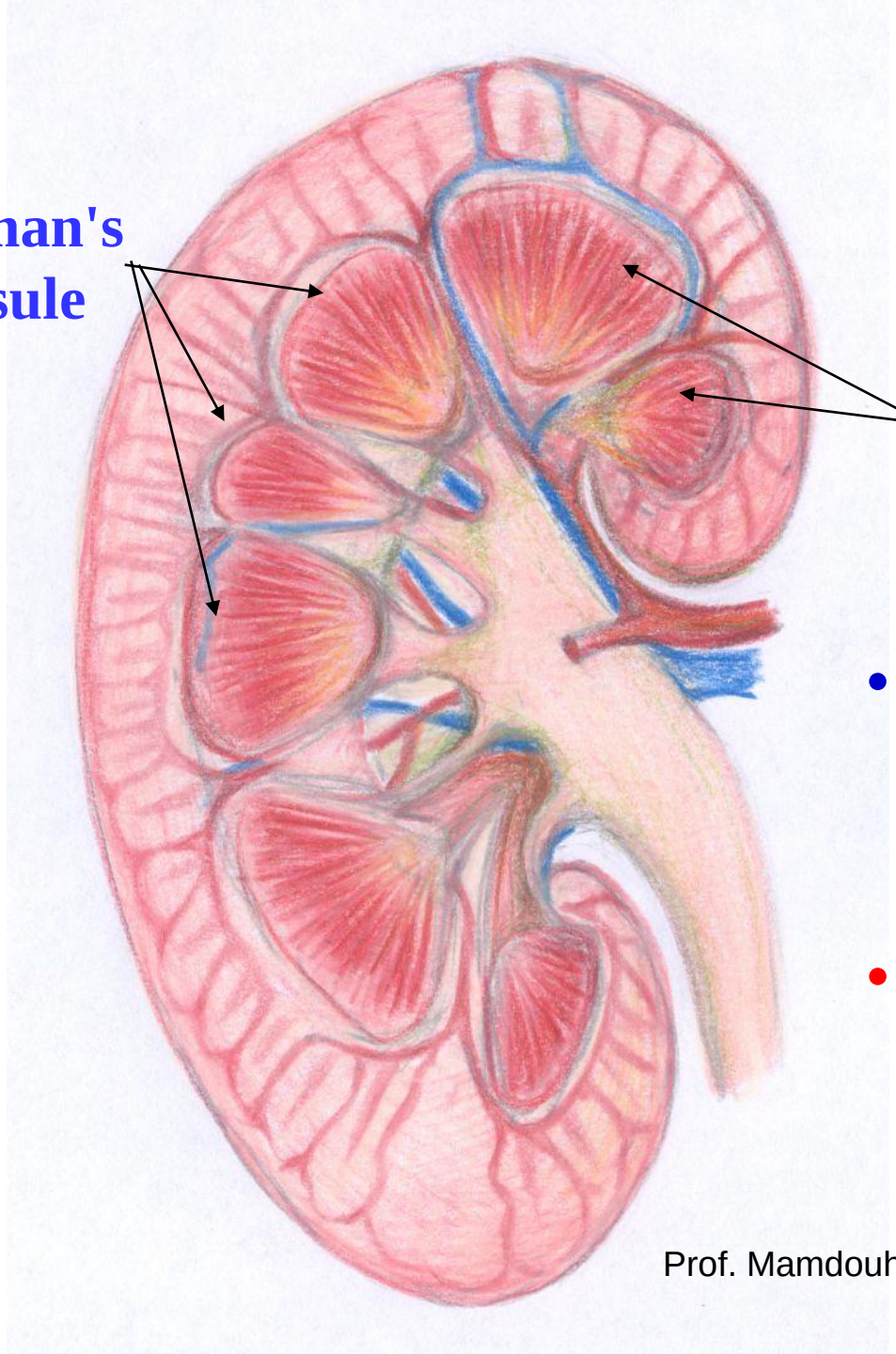

cortex
medulla
calyx
pelvis
renal artery
renal vein
papilla
renal column
pyramid
ureter

Review of Kidney

- The importance of urine formation and excretion as a life-sustaining function is highlighted in cases in which kidney function is suddenly lost.
- Without at least one functioning kidney, death can occur within few days.
- Urine is a very complex fluid comprised of 95% water and 5% solids.
- The approximately 1 to 1.5 liters of urine excreted each day.

The Nephron

- Nephron is the kidney's primary functional unit.
- Each kidney has about 1 million nephrons.
- Each nephron contains a filtering system known as a glomerulus, and a tubule, through which the filtered liquid passes.
- Each glomerulus consists of a capillary network surrounded by a membrane called Bowman's capsule.



- **kidneys act by controlling:**
- **Blood glucose & Blood pressure.**

The Nephron

- The afferent arteriole carries blood from the renal artery into the glomerulus, where it divides to form a circulatory network.
- At the distal end of the glomerulus, the capillaries re-join to form the efferent arteriole through which blood leaves the glomerulus.
- A large amount of circulating blood flows through the kidneys.

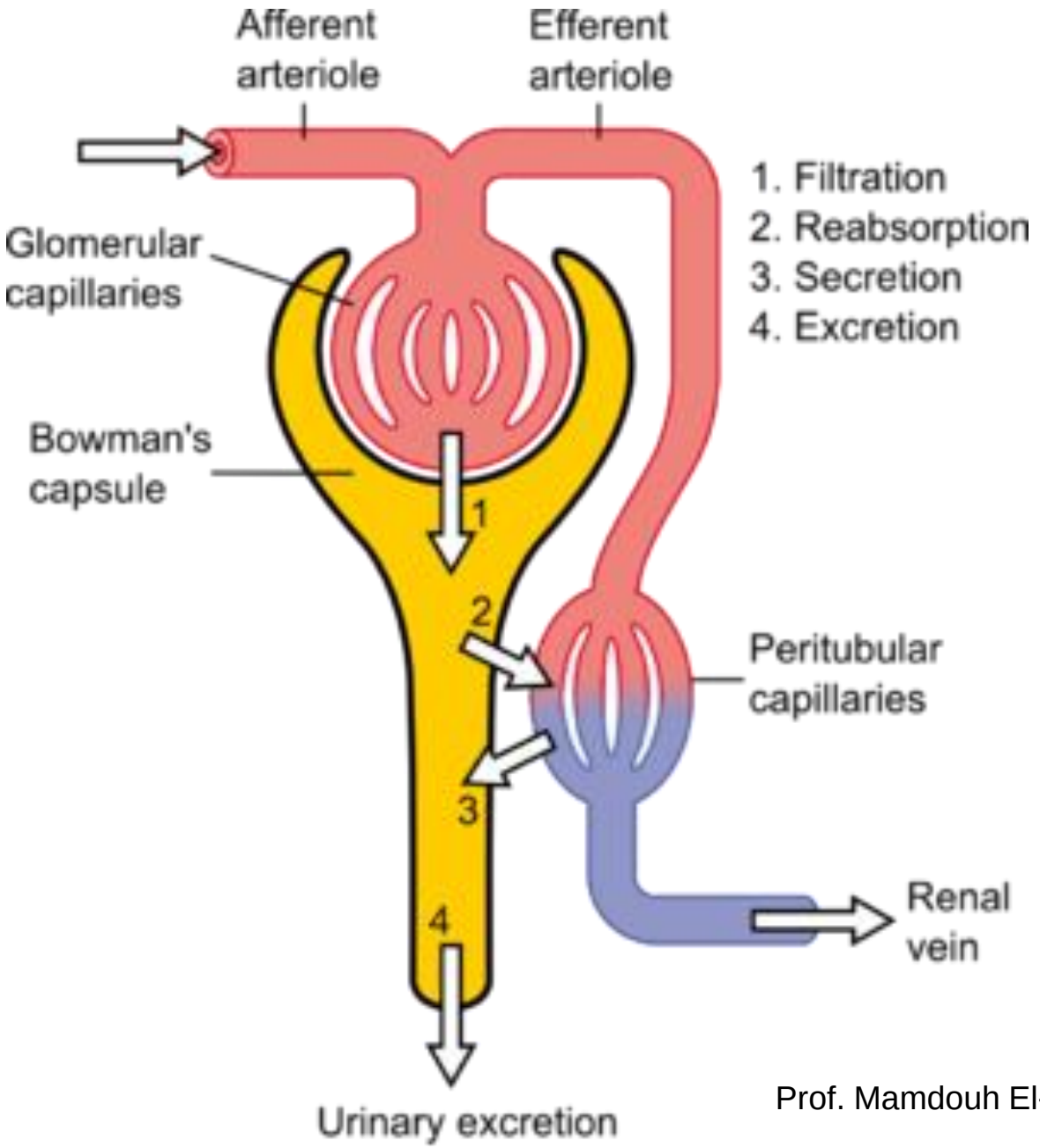
The Nephron

- Approximately 1200 ml of blood per minute is received by the kidneys.
- One liter of urine is the end product of more than 1000 liters of circulating blood processed through the kidneys.
- Kidneys regulate the balance of water and salts in the body, but they also have a very important role in detoxication.

The Main Processes of the Kidney

- **The main processes of the kidney is to take all of the blood in the body and clean it.**
- **This means:**
  1. **Filtering blood to hold back the cells (Ultra-filtration).**
  2. **Reabsorbing much of the filtered water and certain chemicals (Selective Reabsorption).**
  3. **Actively secreting certain chemicals that do not get eliminated by filtration (Direct Secretion).**
  4. **Excretion of urine.**

The 4 processes carried out by the Kidney



Excretion = Filtration – Reabsorption + Secretion

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The Jobs of the Kidney

1. Regulation of water, electrolytes and acid-base balance.
2. Excretion of bi-products: urea, uric acid, creatinine, creatine, sulphate and phosphate.
3. The kidneys are also endocrine organs, producing a number of hormones, and are subject to control by others.

Renal Function

EXCRETORY FUNCTION

Excretion product of the kidney: urine

1- Remove excess fluid

2- Remove waste products

Urea & Creatinine

3- Regulate acid/base balance

4- Regulate electrolyte levels

Hormones Affecting Kidneys

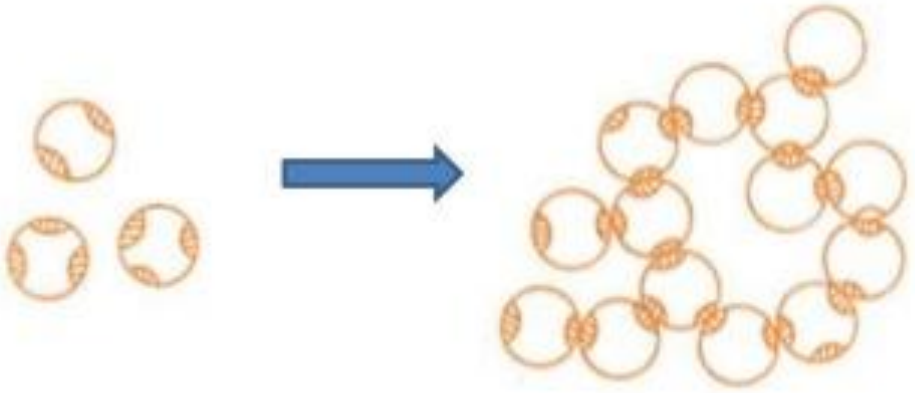
1. **Arginine-vasopressin acts to influence water balance.**
2. **Parathyroid Hormone promotes reabsorption of calcium & phosphate.**

Kidneys as Endocrine Organ

1. **Renin, an enzyme, catalyzes the conversion of angiotensinogen to angiotensin I.**
2. **Erythropoietin a polypeptide hormone promote RBCs synthesis.**
3. **Aldosterone affects sodium reabsorption.**
4. **Activation of 25-Hydroxycholecalcifcrol into 1,25-Dihydroxy-cholecalcifcrol (Calcitriol).**
5. **Thrombopoietin stimulates megakaryocytes to produce platelets.**

Rennin

- is an enzyme found in the stomach of young children
- **Function:**

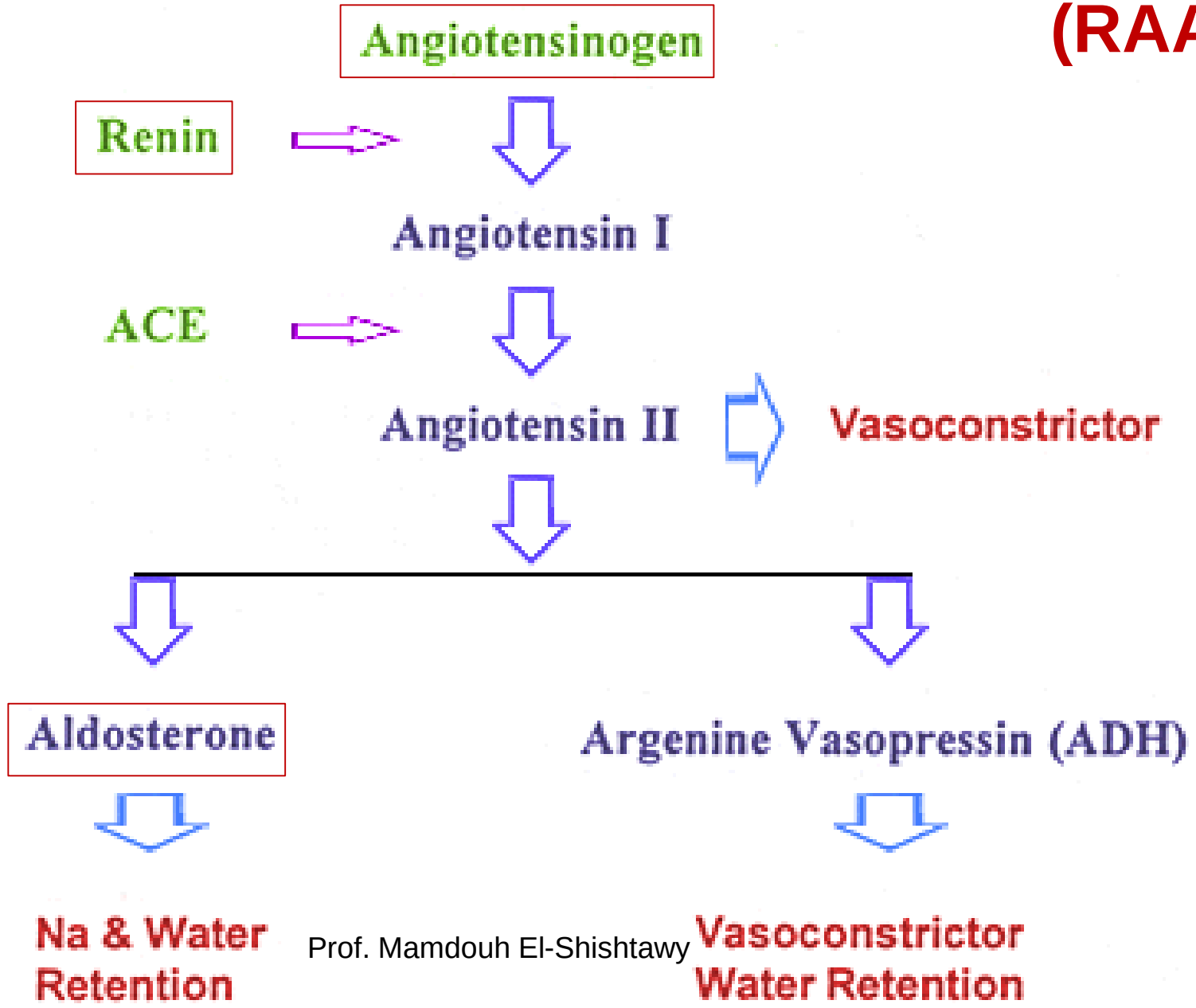


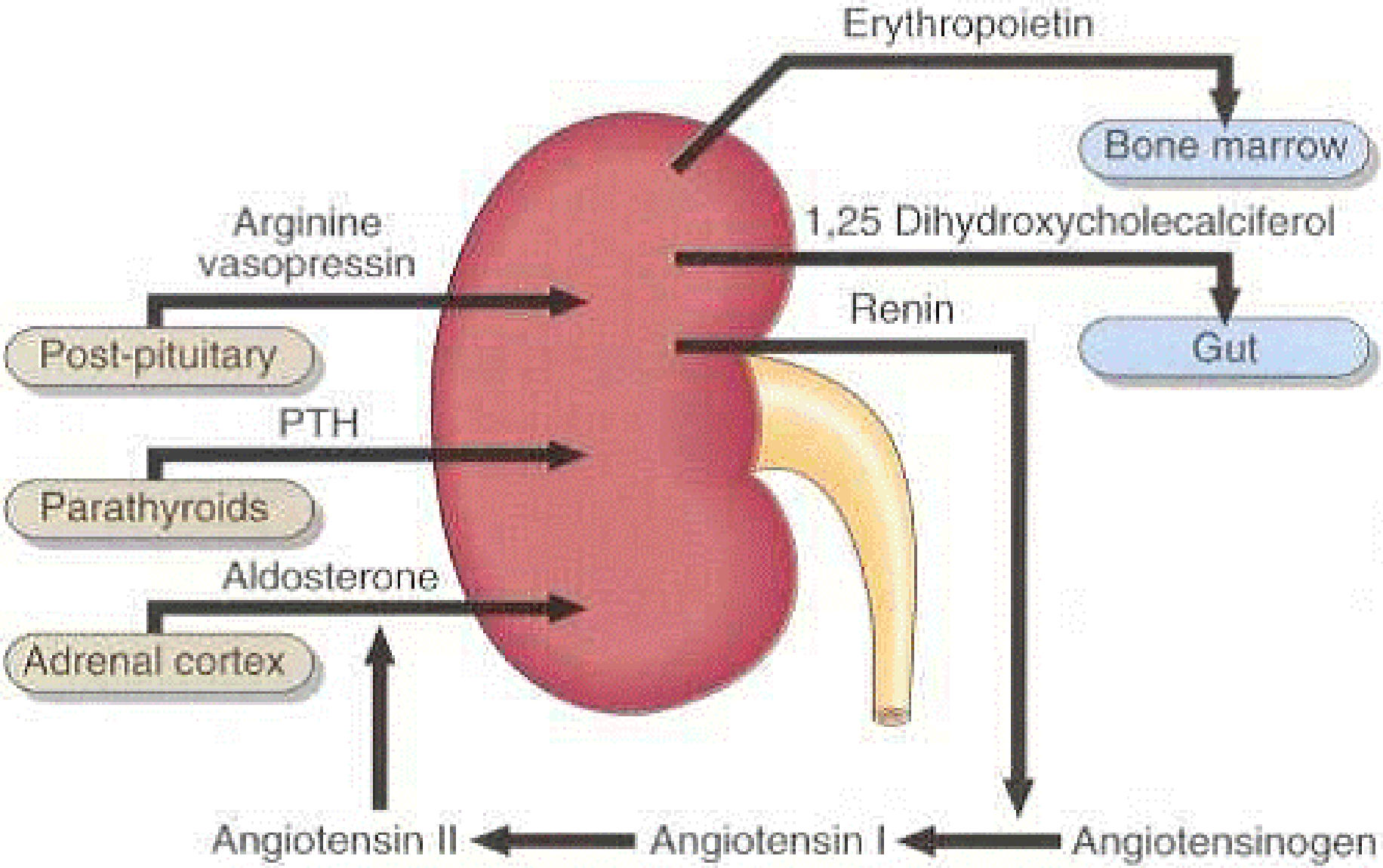
Soluble protein in milk (caseinogen)

Changes into insoluble protein (casein)

Pepsin then acts on the insoluble protein

Renin–Angiotensin–Aldosterone System (RAAS)





Endocrine links in the kidney.

Summary of Chemical Changes of Filtered Blood

Reabsorbed	Secreted
Sugar	Hydrogen ions
Sodium	Potassium
Vitamins	Ammonia
Nutrients	Drugs
Water	Toxins

Composition of Urine

1. **Water (95%).**
2. **Solids: (5%, 50 g/day):**
   a) **Inorganic salts (NaCl) 15 g/day.**
   b) **Organic salts 35 g/day:**
      - ✓ **Pentoses & Glucuronic acid.**
      - ✓ **Enzymes & hormones.**
      - ✓ **Acids:**
        - ✓ **Citric acid,**
        - ✓ **Lactic acid.**
        - ✓ **Aromatic acids.**

Composition of Urine

- ✓ **Non-protein Nitrogenous Compounds (NPN) (30-40 g/day):**
  - ✓ **Urea (25 g/day).**
  - ✓ **Uric acid (0.6 g/day).**
  - ✓ **Creatine & Creatinine (1.4 g/day).**

- **Urea & Uric acid are the main solids secreted.**
- **They must be hydrated to be excreted and so water must excreted with these solids.**
- **Increased solids ⟶ increased urination.**

Urine Collection

- In a clean dry container, free mid stream of urine voided is collected.
- Patient passes some urine into toilet, stops urination, proceeds to urinate into a clean dry container.
- This is allows to cleans up the urethra and the genital area.

Types of Urine Sample Collected

1. **First Morning: more concentrated sample for pathological findings.**
2. **Random: convenient and most common used.**
3. **Post-Prandial: specimen is collected 2–hours after carbohydrate meal, for monitoring of glucose and proteins.**

Types of Urine Sample Collected

4. **24-Hour Sample:**

- **First urine voided, at the early morning – beginning of collection- is discarded.**
- **Then, all urine voided within 24 hours is collected in a large container containing a preservative.**
- **Specimen must be mixed gently each time, for chemical analysis & quantitative results.**

PRESERVATIVES FOR URNIE

- HCL
- TOULENE
- LIGHT PETROLEUM
- THYMOL
- FORMALIN

Preservation of urine sample

- HCl- for 24 hr urinary sample preservation for adrenaline, noradr, **and** steroids.
- Toluene- as a physical barrier
- Boric acid- general preservative
- Thymol- inhibits bacteria, fungi
- Formalin- for preservation of formed elements

Storage of Urine

- **Delay analysis of urine results in:**

1. **Fermentation of urea into ammonia (Increased pH).**
2. **Destruction of glucose by bacteria into lactate (Decreases pH).**
3. **Microbial contamination.**
4. **Degradation of cells and casts.**
5. **Degradation of chemical analysts (Ketones & Bilirubin).**
6. **Oxidation of urobilinogen to urobilin and porpho-bilinogen to prophyrins.**

Changes in Unpreserved Urine

Physical	Change	Cause
Color	Darker	Oxidation of chromogens
Aspect	Increased turbidity	Bacterial growth & crystal pricepitationn.
Odor	Foul smelling	Urea → Ammonia
pH	Increases	Urea → Ammonia

Changes in Unpreserved Urine

Chemical	Change	Cause
Glucose	Decreases	Bacterial fermentation
Ketones	Decreases	Volatilization & Degradation
Bilirubin	Decreases	Exposure to light
Urobilin	Decreases	Oxidation
Nitrite (Pus)	Increases	Bacterial production

Changes in Unpreserved Urine

Microscopic	Change	Cause
RBCs	Lysis	On standing
WBCs	Disintegrate	On standing
Casts	Disintegrate	On standing
Bacteria	Increases	Bacterial proliferation

Kidney Function Tests

- The kidney has a remarkable ability to dilute or concentrate urine, according to an individual's changing physiological needs, and to regulate electrolyte excretion.
- Impaired renal function has adverse effects on blood chemistry, blood pressure, fluid balance, nutrient intake, and the person's general state of health.

Kidney Function Test

- **Blood and urine biochemical tests reflect the extent of the kidney function.**
- **Renal function tests are used to:**

1. **Screen for kidney disease.**
2. **Help determine the cause of kidney disease.**
3. **Determine the extent of renal dysfunction.**

Renal Failure

- Renal failure is the cessation of kidney function.

1. Acute renal failure (ARF), the kidneys fail over a period of hours or days.
2. Chronic renal failure (CRF) develops over months or years and leads eventually to end stage renal failure (ESRF).

- ARF can be reversed and normal renal function regained, whereas CRF is irreversible.

Kidney failure

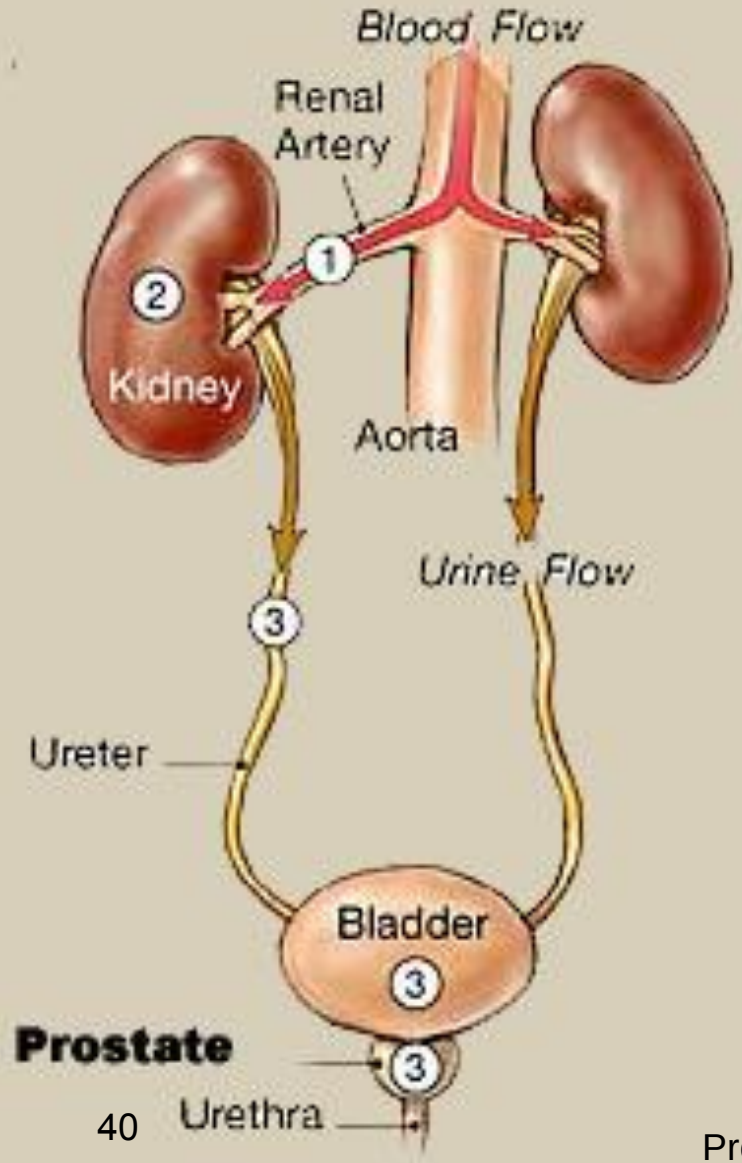
Acute renal failure (ARF)	A sudden loss of kidney function caused by an illness, an injury, or a toxin that stresses the kidneys (kidney function may recover)
Chronic kidney disease (CKD)	A long and usually slow process where the kidneys lose their ability to function
End-stage renal disease (ESRD)	When the kidneys have completely and permanently shut down

Acute Renal Failure

- **Renal failure is a loss of renal function characterized by uremia.**
- **Causes of Acute Renal failure is:**

1. **Pre–renal.**
2. **Renal.**
3. **Post–renal failure.**

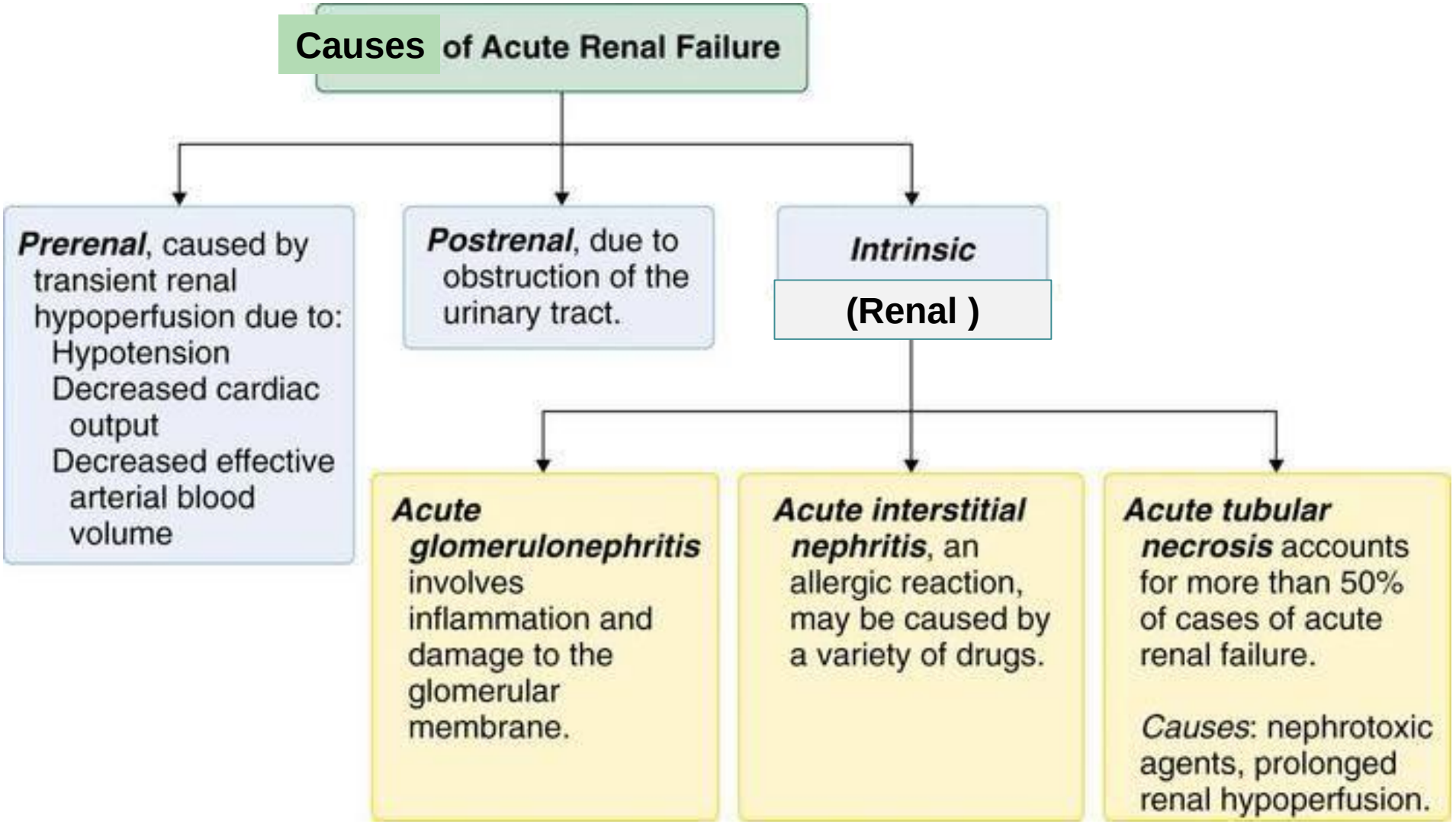
Causes of Acute Renal Failure



1 Prerenal
Sudden and severe drop in blood pressure (shock) or interruption of blood flow to the kidneys from severe injury or illness **or congestive heart failure (CHF).**

2 Intrarenal
Direct damage to the kidneys by inflammation, toxins, drugs, **viral** infection,

3 Postrenal
Sudden obstruction of urine flow due to enlarged prostate, kidney stones, bladder tumor, or injury


Causes of Acute Renal Failure
Prerenal, caused by transient renal hypoperfusion due to:
Hypotension
Decreased cardiac output
Decreased effective arterial blood volume
Postrenal, due to obstruction of the urinary tract.
Intrinsic
(Renal)
Acute glomerulonephritis involves inflammation and damage to the glomerular membrane.
Acute interstitial nephritis, an allergic reaction, may be caused by a variety of drugs.
Acute tubular necrosis accounts for more than 50% of cases of acute renal failure.
Causes: nephrotoxic agents, prolonged renal hypoperfusion.

Urinary Symptoms of Kidney Failure

Glomerular Filtration Rate (GFR)

- The rate at which plasma is filtered by the kidney glomeruli.
- An important measurement in the evaluation of kidney function
- GFR = 125 mL plasma/min or, 180 L/day
- Plasma volume (70-kg young adult man) = about 3L, the **kidneys filter the plasma some 60 times in a day.**

5 L → 36 times

Significance of Glomerular Filtration Rate

- The glomerular filtrate is an ultra-filtrate of plasma, and has the same composition as plasma without most of the proteins
- A normal Glomerular Filtration Rate (GFR) will depends on renal blood flow[1] and blood pressure.[2]
- GFR is directly related to body size,[3] and consequently is higher in men than women.
- It is also affected by age,[4] declining in the elderly.[5]

Tests of Glomerulus Function

- **GFR falls due to:**

1. **Reduction of the renal blood supply or,**
2. **Destruction of nephron by renal disease.**

- **Falls of GFR lead to retention of the waste products of metabolism in the blood [elevation in serum urea (uremia) and creatinine].**

Measurement of GFR: Renal Clearance

- The amount of substance excreted can be calculated by measuring the urinary concentration (U) and multiplying that by the volume of urine collected in a given time (V, liters in a 24 h period).
- Thus, the Urinary excretion rate = U x V.
- The volume of plasma which would have contained that amount can be worked out by dividing the amount excreted (U x V) by the plasma concentration of the substance (P).

Renal Clearance

- **Renal Clearance = $\frac{U \times V}{P}$**
- **Urinary concentration (U)**
- **Volume of urine (V)**
- **Plasma concentration of the substance (P).**
- **This is the volume of plasma which would completely 'cleared' of the substance in the given time for the amount seen in urine.**
- **The maximum rate that the plasma can be cleared of any substance, the 'clearance' is equal to the GFR.**

Renal Clearance calculation

$$C_s \times P_s = U_s \times V$$

$$C_s = \frac{U_s \times V}{P_s}$$

$$\text{Clearance} = \frac{\text{urinary excretion rate}}{\text{plasma concentration}}$$

C_s – clearance rate of a substance s

P_s – plasma concentration of the substance

V – urine flow rate

U_s – urine concentration of the substance

8th Lecture

1. Creatinine Clearance

- An estimate of the GFR can be calculated from the creatinine content of a 24 hour urine collection, and the plasma concentration within this period.
- Normal Creatinine Clearance = 100 ± 20 ml/min.
- Creatinine clearance is directly related to the GFR provided that:
  1. The urine volume is collected accurately.
  2. There are no ketones or heavy proteinuria.

1. Creatinine Clearance

- The decrease in creatinine clearance is a very sensitive indicator of a decreased GFR that may be a result of:
  1. Acute or chronic damage to the glomeruli.
  2. Reduced blood flow to the glomeruli.
- Now, creatinine clearance can be calculated depending on age (years), weight (Kg) in addition to serum creatinine (μmol/L).

1. Creatinine Clearance

$$\text{Creatinine clearance (mL/min)} = \frac{(140 - \text{age [years]}) \times \text{weight [kg]}}{\text{serum creatinine [}\mu\text{mol/L]}} \quad \text{(Females)}$$

$$\frac{(140 - \text{age [years]}) \times \text{weight [kg]} \times 1.2}{\text{serum creatinine [}\mu\text{mol /L]}} \quad \text{(Males)}$$

2. Serum Creatinine

- **Normal Level: up to 1.4 mg/dl**
- **Creatinine is a waste product formed in muscle from a high energy storage compound, creatine phosphate.**

2. Serum Creatinine

- **The amount of creatinine excreted per day is a function of the muscle mass and is not affected by:**
  1. **Diet,**
  2. **Age,**
  3. **Sex, or**
  4. **Exercise.**
- **Its amount is 1–2 g/day for an adult.**
- **Women excrete less creatinine than men because of their smaller muscle mass.**

2. Serum Creatinine

- **Creatinine appears in the glomerular filtrate and is not reabsorbed by the tubule; hence, any condition that reduces the glomerular filtration rate will result in a decreased excretion from the body, with a consequent rise in plasma creatinine.**

Significance of Serum Creatinine

1. Since the excretion rate of creatinine is relatively constant.
2. Creatinine production is not influenced by protein catabolism or other external factors.

- So, the concentration of creatinine in the serum is a good measure of renal glomerular function.
- Serum Creatinine is increased in:
  1. Significant reduction in GFR or,
  2. When urine elimination is obstructed.

3. Serum Urea

- **Normal Level: 15–50 (20–40) mg/dl.**
- **The α-amino group of all amino acids are broken down in the mammalian body giving urea.**
- **Urea represents the end-product of amino acids metabolism.**
- **Urea is a waste product that is soluble in water and excreted solely by the kidney.**

3. Serum Urea

- So, serum urea concentration is influenced by factors not connected with:

1. Renal function or,
2. Urine excretion.

- It is affected strongly by the degree of protein catabolism, whether produced by:

1. High protein diet or,
2. Hyper-secretion of adrenal steroids or,
3. Injection of adrenal steroids that results in the mobilization of protein for energy purposes.

3. Serum Urea

- The various pre-renal, renal, and post-renal factors that affect the concentration of serum creatinine also influence the level of serum urea.
- For these reasons, the measurement of serum creatinine is a better indicator of kidney status than is that of urea.

3. Serum Urea

- **Serum Urea is increased in:**

1. **High protein diet,**
2. **Administration of cortisol-like steroids,**
3. **Stressful situations.**

- **Serum Urea is decreased in:**

1. **Late pregnancy when the fetus is growing rapidly and utilizing maternal amino acids,**
2. **Starvation, and**
3. **In patients whose diet is grossly deficient in proteins.**

4. Serum Uric Acid

- **Uric acid is the end product of purine catabolism.**
- **It circulates in plasma as sodium urate and is excreted by the kidney.**
- **Serum uric acid is not used as a primary test for the evaluation of kidney function because creatinine and/or urea serve this purpose much better.**
- **Urate deposition in the kidney may lead to renal failure.**

4. Serum Uric Acid

- **Normal Levels of Serum Uric Acid:**
  - **Male: 4.0 – 7.0 mg/dl.**
  - **Female: 3.0 – 6.0 mg/dl.**

4. Serum Uric Acid

- **Increased (Hyperuricemia) in:**

1. **Gout.**
2. **Renal disease.**
3. **von Gerick's disease.**
4. **After increased breakdown of nucleic acids, as:**
   a) **Leukemia.**
   b) **Toxemia of pregnancy.**
   c) **Massive irradiation of tumors.**
   d) **Chemotherapy (Cytotoxic drugs).**

4. Serum Uric Acid

- **Decreased in:**

1. **After administration of ACTH.**
2. **Cortisol-like steroids.**
3. **Drugs that decrease reabsorption of urate by renal tubules, as:**
   a) **Aspirin.**
   b) **Probenecid.**
4. **Allopurinol that blocks uric acid synthesis.**

Gout (Hyperuricemia)

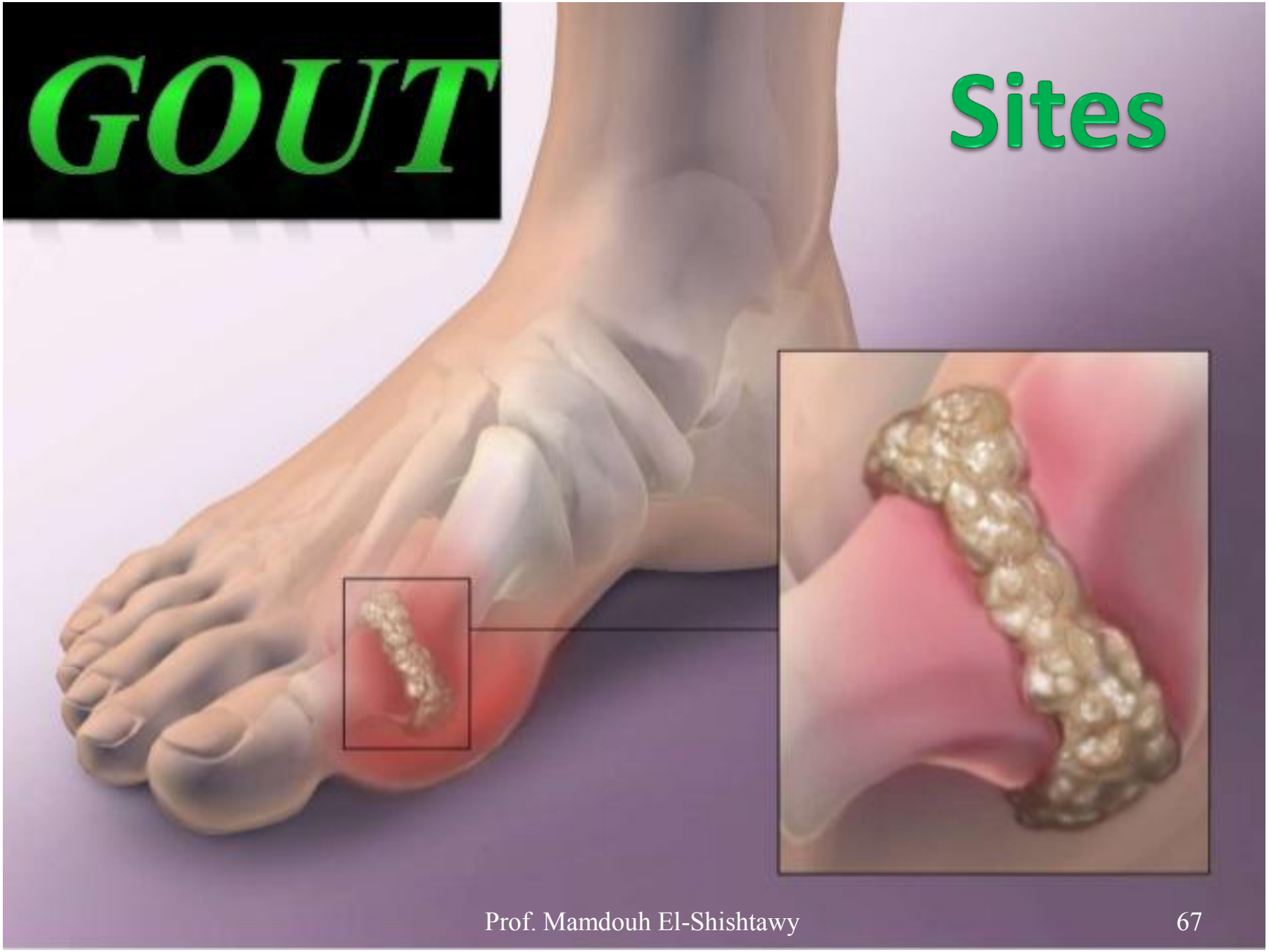
- **It is a disorder characterized by high levels of uric acid in blood, because of either high production or under–excretion of uric acid or Combination of the two processes.**
- **Hyperuricemia results in the deposition of crystals of mono–sodium urate.**

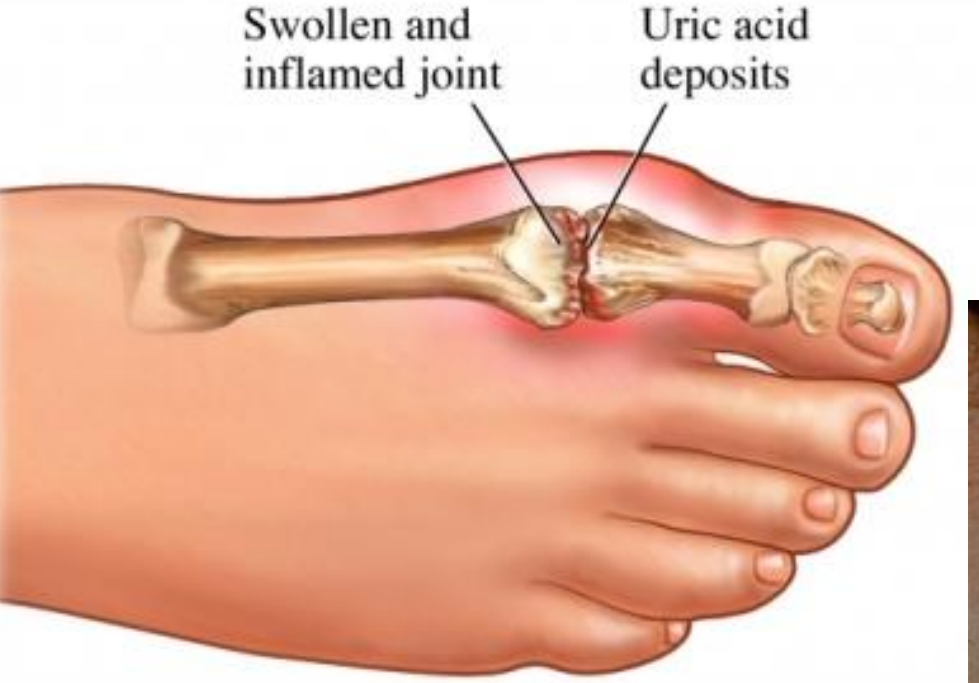
Gout

- **Prevails (يسود) mainly in adult males.**
- **Rarely encountered in premenopausal women.**
- **Usually affect the kidneys and joints in the lower extremities (the big toe is the classic site).**

GOUT

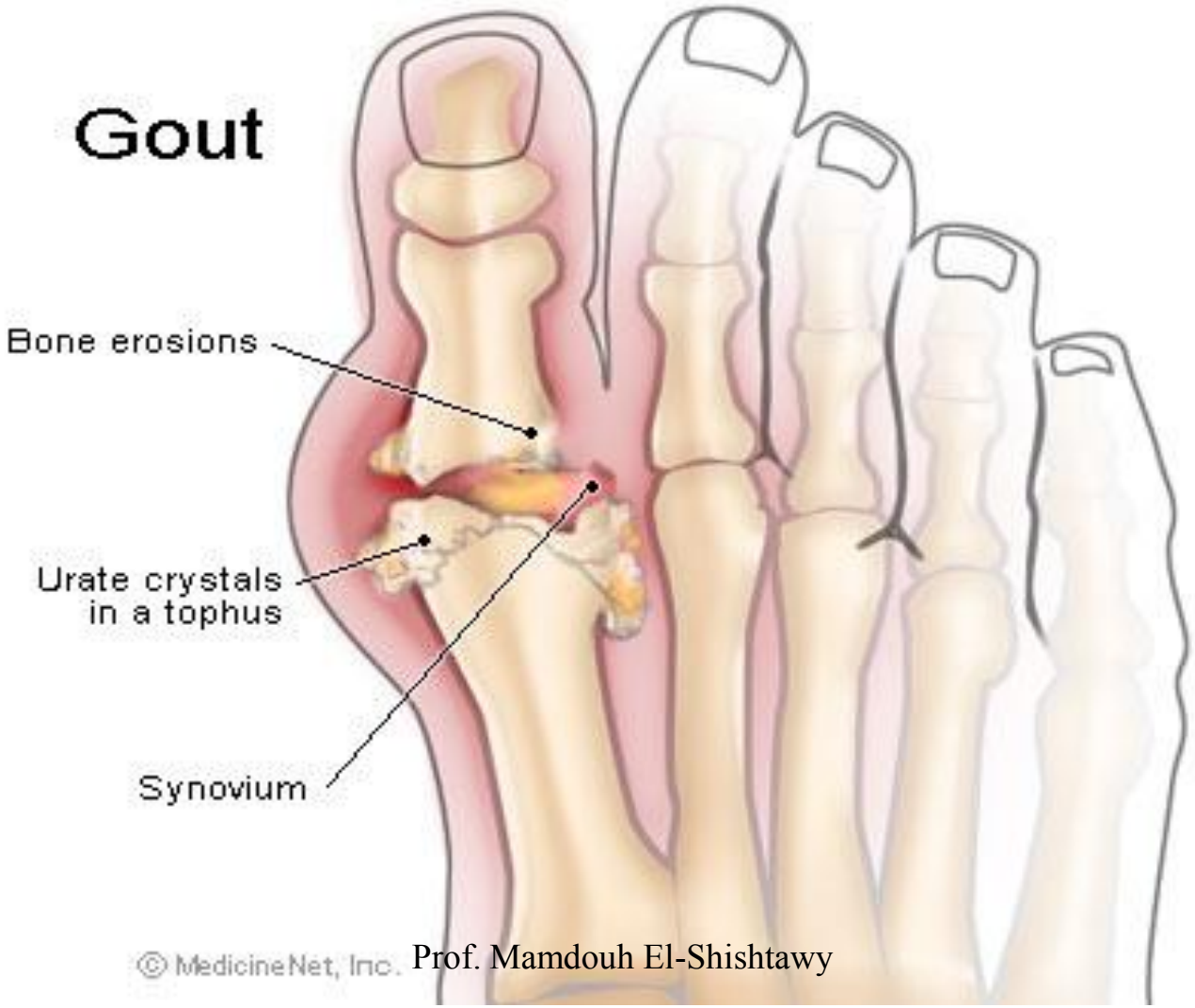
Sites





- **Pain is usually severe; joint may be inflamed, swollen, red and hot.**

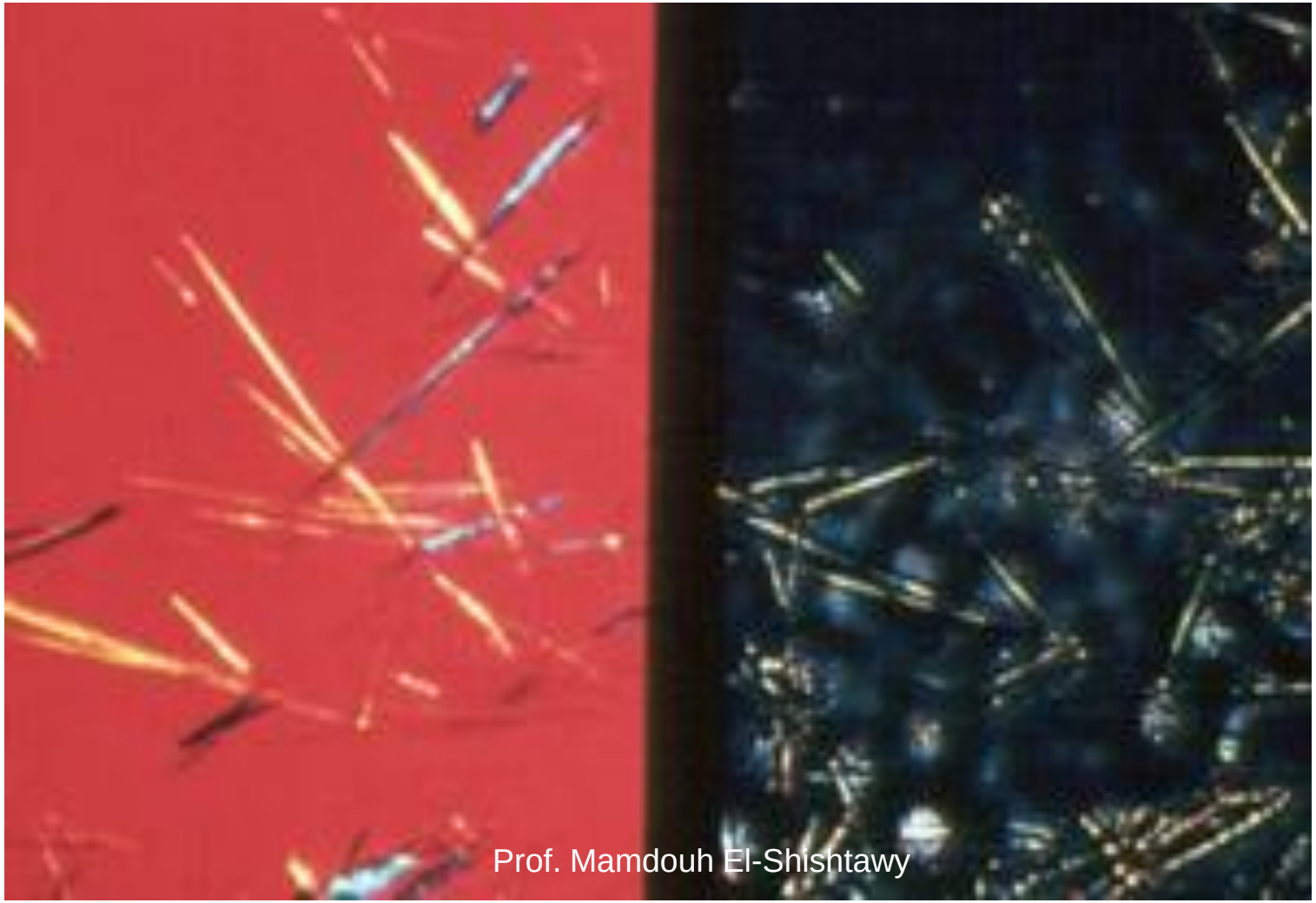
Silent tissue deposition & Hidden Damage



Sites

Can occur in other joints, bursa & tendons

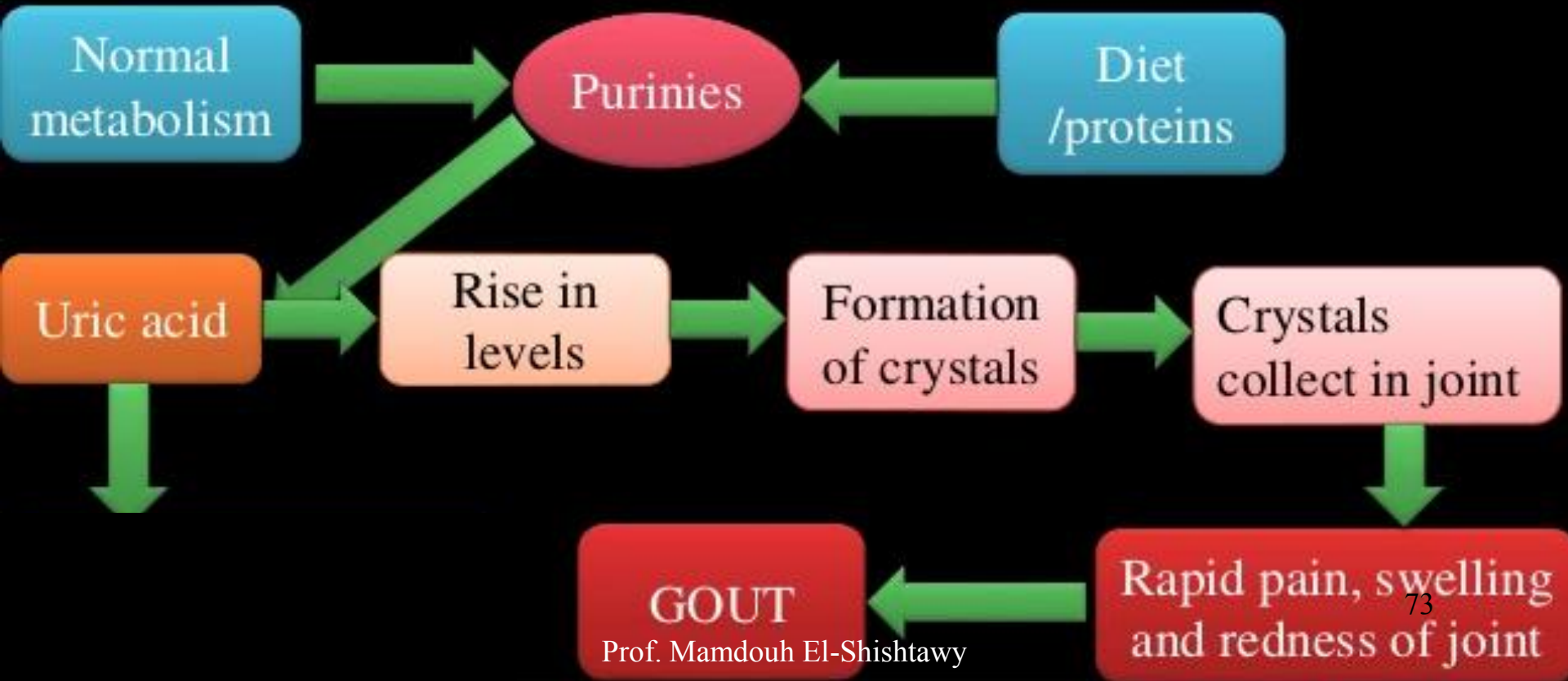
SYNOVIAL FLUID



TOPHI

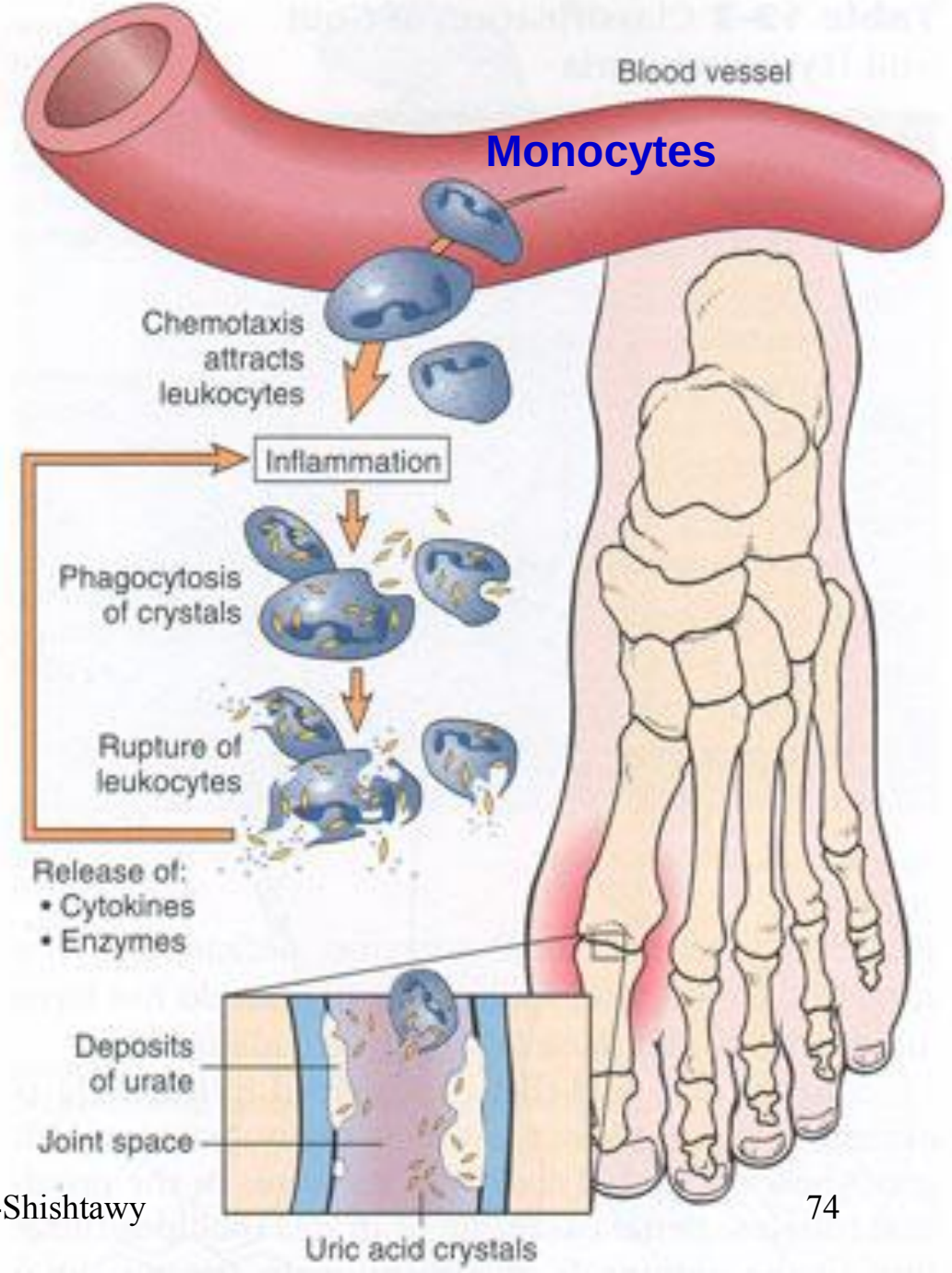
In severe hyperuricemia, crystals of sodium urate deposited in the soft tissues, particularly in the joints. Such deposits commonly known as Tophi.

CAUSES OF GOUT:



Gout

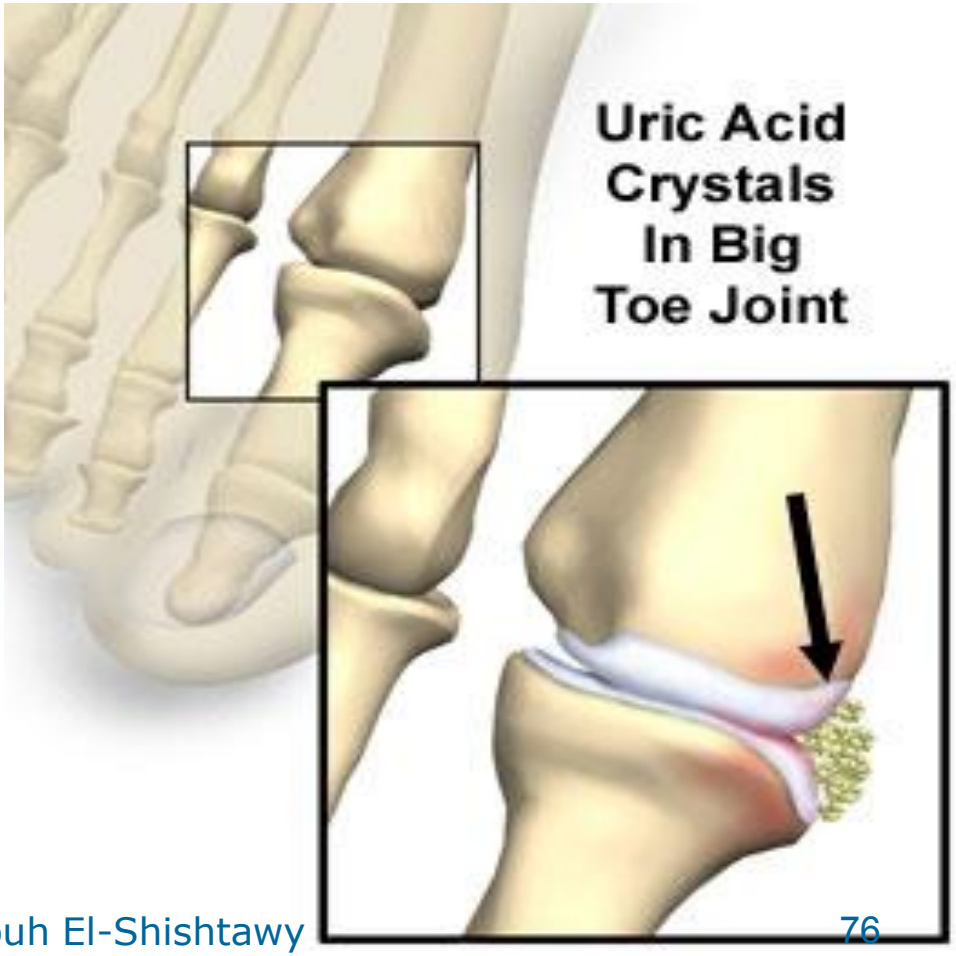
- **The deposition of uric acid crystals, initiates an chemotaxis and inflammatory process involving the infiltration of granulocytes that phagocytized the urate crystals.**



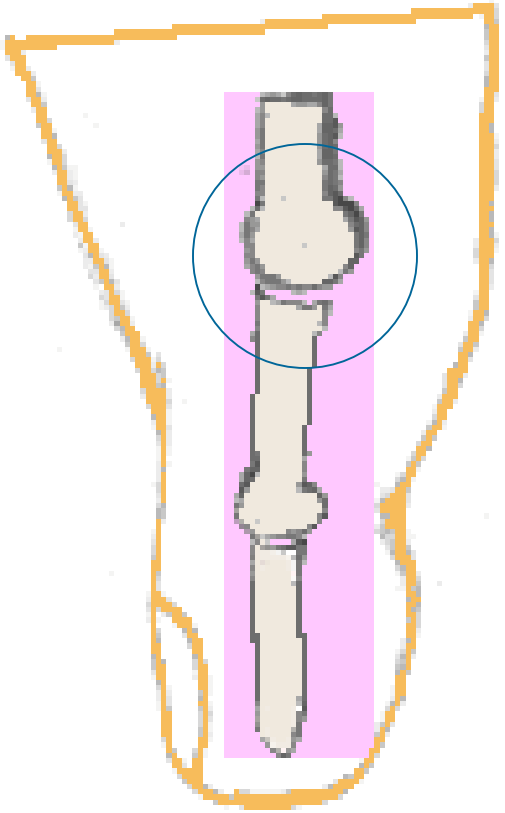
Symptoms of Gout

1. Painful Joints

2. Painful Big Toe



3. Acute Attack



Pain, red, swollen, hot

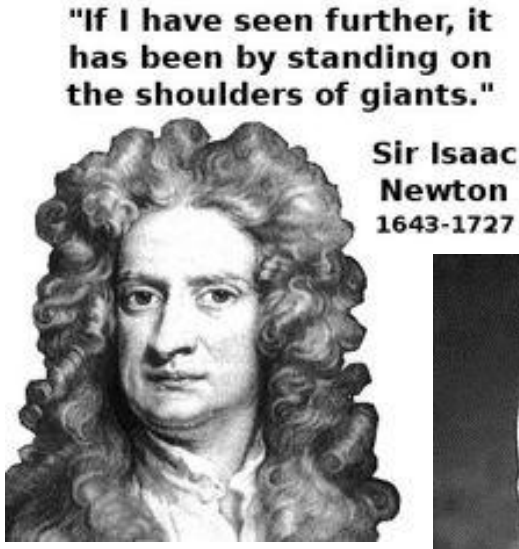
Subcutaneous or periarticular nodules

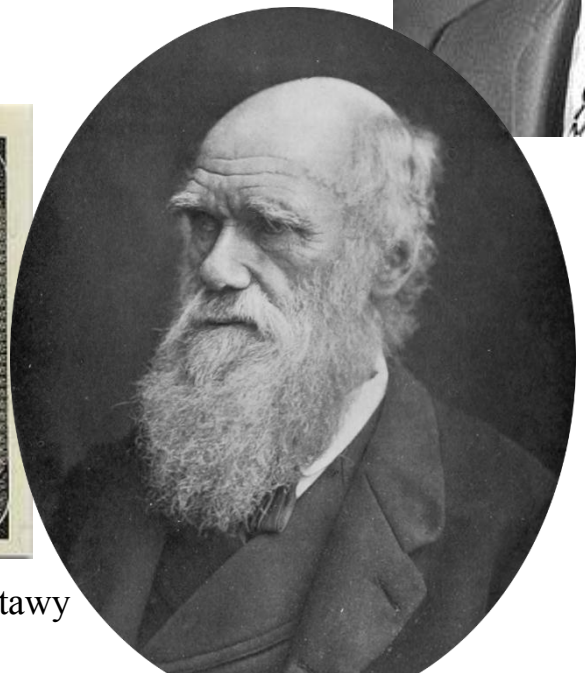
3. Acute Attack

4. Overhanging edge of cortex & erosion of bone with sclerotic borders

GOUT

- **People with gout:**
  1. **Isaac Newton.**
  2. **Benjamin Franklin.**
  3. **Martin Luther King.**
  4. **Charles Darwin.**





Drugs may Induce Hyperuricemia

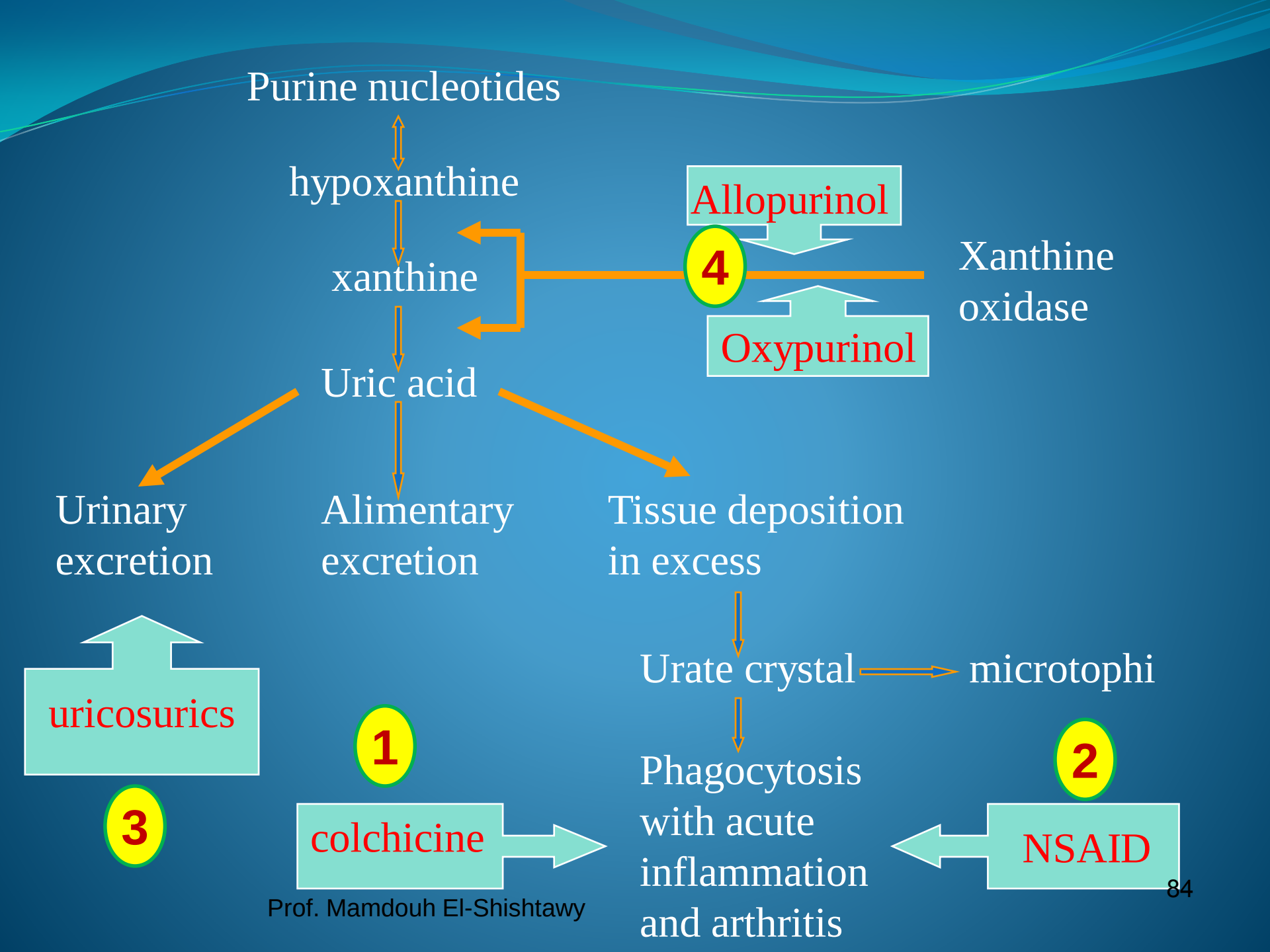
1. Niacin
2. Thiazides and other diuretics
3. Low dose aspirin
4. Pyrazinamide (Antituberculous)
5. Ethambutol
6. Cyclosporine
7. Cytotoxic drugs

Non–Pharmacological Approaches

1. **Avoid purine rich foods:**
   a) **Red meat and organ meat (liver, kidneys).**
   b) **Shellfish, anchovies (أنشوجة), mackerel, herring (سمك رنجة).**
   c) **Meat extracts and gravies (المرق والشوربة).**
   d) **Peas and beans, lentils.**
   e) **Beer, other alcoholic beverages.**
2. **Weight loss.**
3. **Control alcohol (binge drinking).**

Treatment of Gout (Management Strategy)

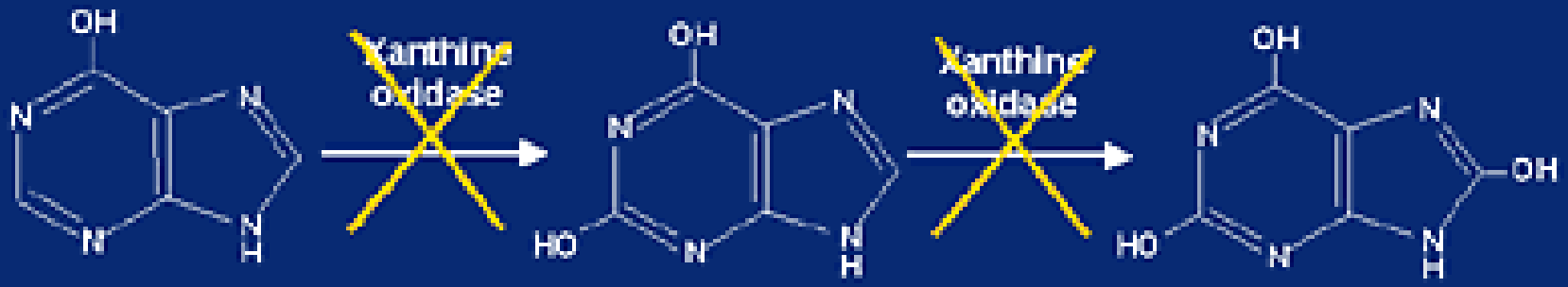
1. **Colchicine: decreases the movement of granulocytes into affected area (Inhibit chemotaxis).**
2. **Analgesics (NSAIDs as Indomethacin).**
3. **Uricosuric agents: (Increasing urinary excretion by inhibiting reabsorption), as probenecid.**
4. **Xanthine oxidase inhibitors: as allopurinol.**
5. **Increase uric acid solubility in urine: as piperazine hydrate.**


Purine nucleotides
hypoxanthine
xanthine
Uric acid
Allopurinol
4
Xanthine oxidase
Oxypurinol
Urinary excretion
Alimentary excretion
Tissue deposition in excess
Urate crystal
microtophi
uricosurics
3
1
colchicine
Phagocytosis with acute inflammation and arthritis
2
NSAID

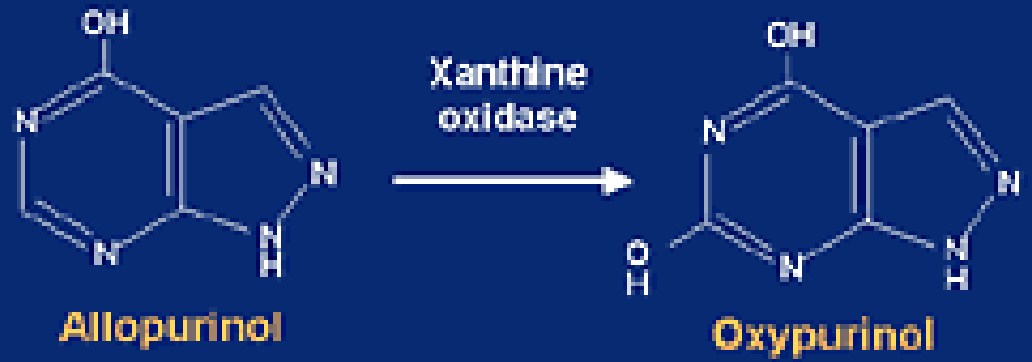
Allopurinol mechanism of action

Urate-Lowering Agents
Allopurinol

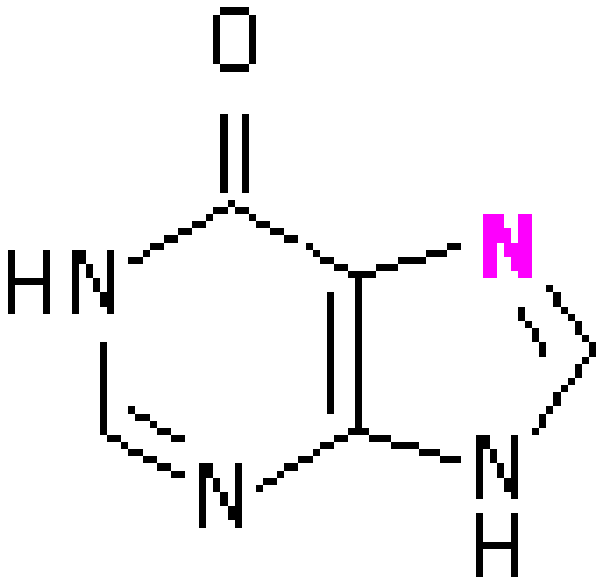
Allopurinol and oxypurinol block the conversion of hypoxanthine to xanthine to uric acid



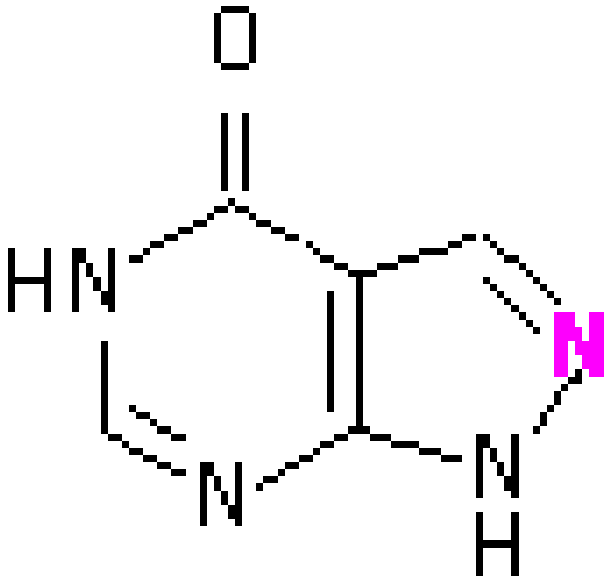
Allopurinol and metabolite oxypurinol are purine analogs and both substrates and inhibitors of xanthine oxidase



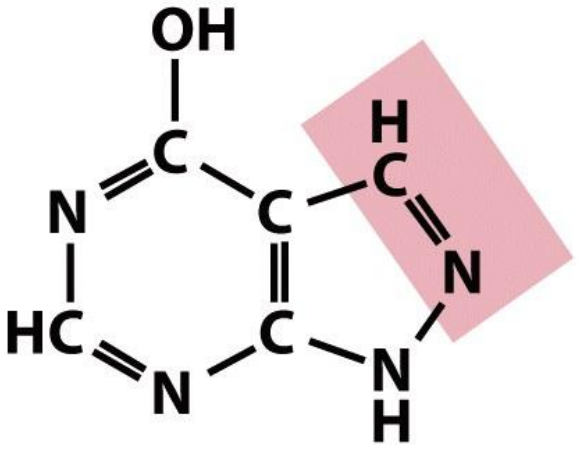
- **Allopurinol competitively inhibits Xanthine oxidase enzyme**



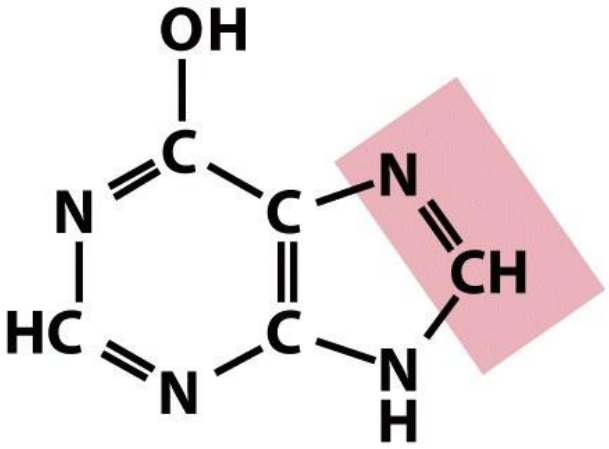
Hypoxanthine



Allopurinol

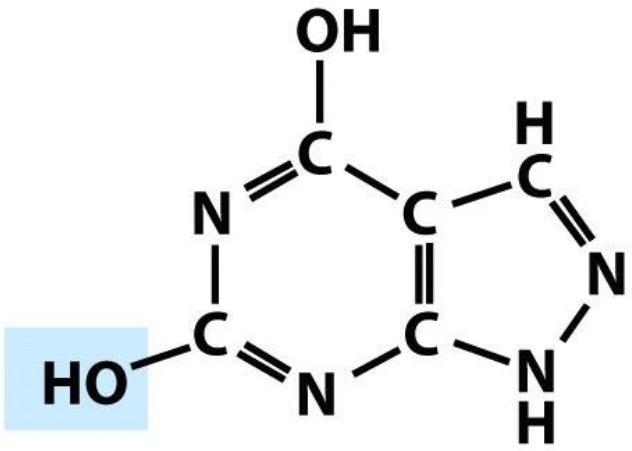


Allopurinol



Hypoxanthine
(enol form)

xanthine
oxidase



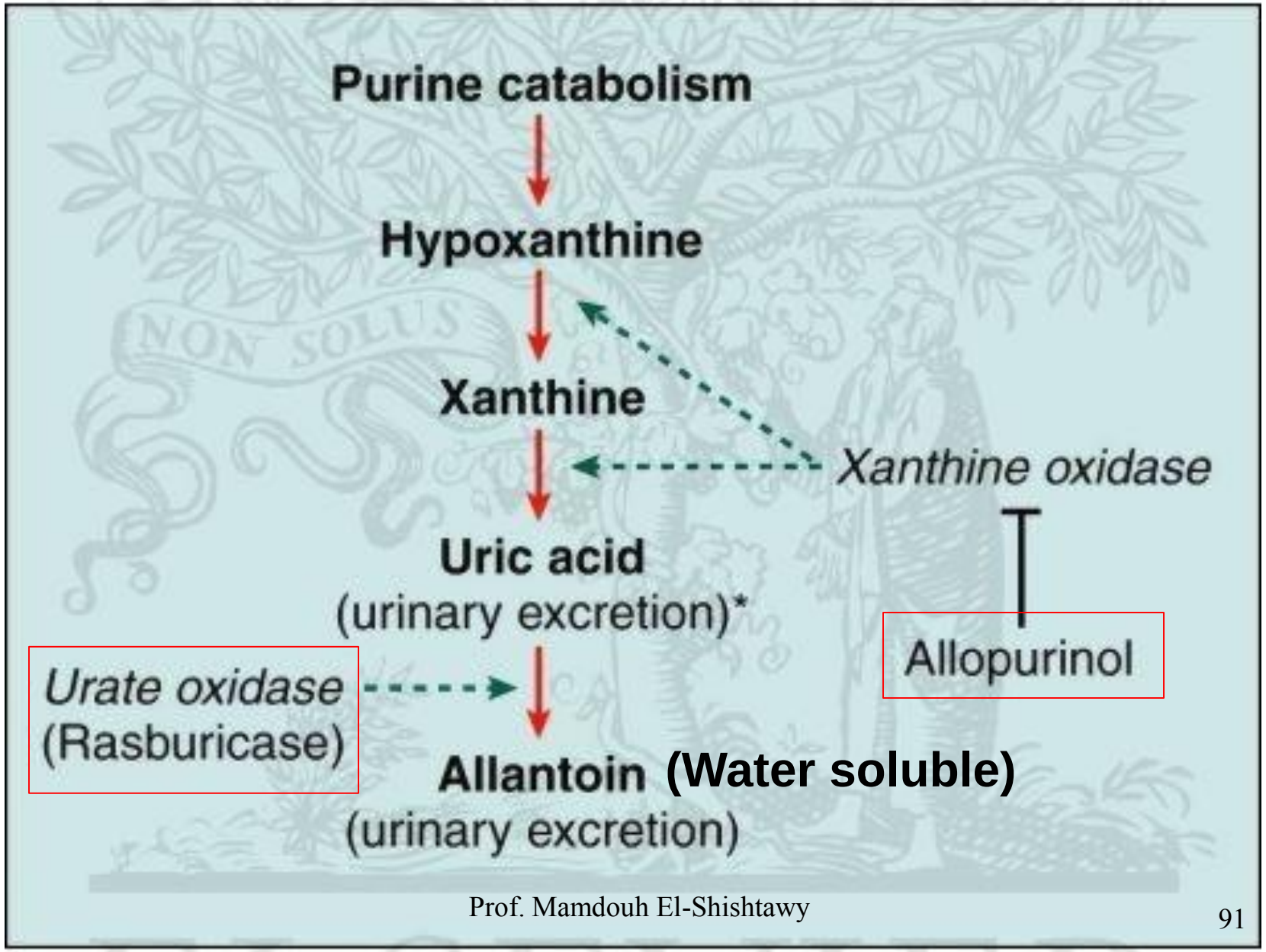
Oxypurinol

Allopurinol

1. **Prevents attack of gouty arthritis.**
2. **Prevents attack of nephropathy.**
3. **Used during chemotherapy of cancer.**
4. **Prevents recurrent calcium oxalate calculi (tophi).**
5. **Inhibits the metabolism of certain anticancer drugs (Azathioprine).**

Rasburicase (Elitek), Genetic Engineering

- A recombinant form of urate oxidase (Uricase), an enzyme that converts uric acid to allantoin.
- It is used for initial management of plasma uric acid levels in pediatric patients with leukemia, lymphoma, and solid tumor malignancies who are receiving anticancer therapy expected to result in elevation of plasma uric acid.
- It is very efficacious in the reduction of the risk of renal damage during chemotherapy.
- It can dissolve uric acid crystals and can improve renal functions, permitting to continue chemotherapy.


Purine catabolism
Hypoxanthine
Xanthine
Xanthine oxidase
Uric acid
(urinary excretion)*
Allopurinol
Urate oxidase
(Rasburicase)
Allantoin (Water soluble)
(urinary excretion)

السلام عليكم